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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,804	09/14/2006	Norio Nakatsuji	3190-099	9728

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KILYK & BOWERSOX, P.L.L.C.
400 HOLIDAY COURT
SUITE 102
WARRENTON, VA 20186

EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	**PAPER NUMBER**
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,804	NAKATSUJI ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *10 and 19-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/7/06, 10/23/06, 7/2/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 as submitted 2/19/08 are currently pending.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-9 and 11-18, in the reply filed on 3/30/09 is acknowledged. Applicant's election without traverse of the species "collagen," "epithelial cell growth factor," and "fetal lung fibroblasts" in the same reply is also acknowledged.

Claims 10 and 19-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/30/09.

Examination on the merits will commence at this time on claims 1-9 and 11-18 ONLY, to the extent they read on the elected species where applicable.

Claim Objections

Claims 6 and 13-16 are objected to because of the following informalities: They appear to omit the word "of" after the word "proliferation" in line 3 of each claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 and 11-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a medium “wherein the amount of serum albumin is from 2g/L to 50g/L," which is confusing for several reasons. First, it is not clear that the units “g/L” refer to “g serum albumin per liter of medium.” Also, the phrasing of the claim does not clearly recite a range. The requirements for insulin suffer similar deficiencies. Clarification is required. The examiner suggests the language, "a medium containing between 2g and 50g serum albumin and between 1mg and 100mg insulin per liter of medium.”

The language “at least one kind selected from” in claims 1, 3, 5, 6, 8, and 13-16 is queried, since it is not clear whether the component in question is necessarily one from the following list or whether a component that is closely related to the species on the list. The examiner suggests applicant employ standard Markush-type language, i.e. "a basal medium selected from the group consisting of MEM, ... and MCDB 202,” e.g. See M.P.E.P. § 2173.05(h).

Because claims 2-9 and 11-18 depend from indefinite claim 1 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 2 and its dependents are queried, because they require that the medium *per se* contain a cell adhesion factor such as collagen. However, all of the working examples appear to describe a system in which cells are cultured on a culture dish

coated with the cell adhesion factor, not one in which the cell adhesion factor is present within the media.

Claims 6 and 13-16 are drawn to a method for preparation of feeder cells for embryonic stem cells, but it is not clear which steps in the claims as recited are necessary to achieve this end. Claim 6, for example, requires "culture and proliferation [of] a cell population ... in the culture medium **for preparation of feeder cells for embryonic stem cells** according to claim 1, and inactivation of proliferation …" It is not clear whether the bolded portion of the claim refers to the medium of claim 1 or to the end point of claim 6. Clarification is required. The examiner suggests that the first step refer merely to "the medium of claim 1" and that the claim include a requirement that the inactivation of proliferation is necessary for the preparation of feeder cells, e.g. "inactivation …, thereby yielding feeder cells for embryonic stem cells."

Claims 9, 17, and 18 require that the cells in the method undergo division "twenty or more times on average." It is not clear whether the "average" refers to the number of divisions within a single culture vessel or to the number of divisions in numerous culture vessels over time. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Snodgrass (2002, U.S. Patent Application Publication 2002/0012905; reference A).

Snodgrass teaches a culture medium containing 0.4% bovine serum albumin (BSA, i.e. 4g BSA/L medium) and between 0.1 and 100μg insulin/mL medium (i.e. between 0.1 and 100 mg insulin/L medium) in a basal medium such as RPMI 1640, Ham's F10, or Ham's F12 (paragraph 137).

M.P.E.P. § 2111.02 reads, "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." As such, the limitation "a medium for preparation of feeder cells for embryonic stem cells" does not affect the patentability of the claimed composition/method. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6-9, 11-15, 17, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al. (2002, U.S. Patent Application Publication 2002/0031828; reference B) taken in view of Goodheart (2004, U.S. Patent Application Publication 2004/0023322; reference C), Hook et al. (2004, U.S. Patent Application Publication 2004/0214282, reference D), Reich (1990, U.S. Patent 4,973,466; reference E), and Benedict et al. (1992, U.S. Patent 5,108,923; reference F).

Yamamoto teaches a method for culturing 3T3 mouse embryonic lung fibroblasts in a medium containing fetal bovine serum (FBS, which contains growth factors; paragraph 30). Yamamoto teaches that feeder layers may be yielded by sterilizing the fibroblasts by irradiation or addition of mitomycin C (paragraph 3).

Yamamoto does not teach a medium containing the claimed amounts of BSA and insulin and does not specifically suggest using the basal media listed in claim 1. Yamamoto does not teach culturing lung fibroblasts in a system containing collagen. Yamamoto does not specifically indicate how many divisions the 3T3 cells should undergo prior to being inactivated.

Goodheart teaches a medium for growing MRC-5 cells (human fetal lung fibroblasts) in Medium 199 supplemented with 10mg insulin/L of medium (paragraph 59). Goodheart teaches that the amount of insulin in the media may vary and specifically contemplates varying the components in the media (paragraphs 59 and 60).

Hook teaches a medium for growing MRC-5 cells in Medium 199 containing 0.2% BSA (i.e., 2g BSA/L medium) and insulin (paragraph 101). Hook teaches culturing MRC-5 cells on culture dishes coated with collagen (paragraph 100); because the medium of Hook is contacted with the collagen-coated dishes, the medium can be reasonably interpreted as "comprising collagen."

Reich teaches that insulin is a mitogen, i.e. that it promotes cell division (ccolumn 6, lines 1-8).

Benedict teaches that FBS contains BSA (column 9, lines 57-58). Benedict teaches that both BSA and FBS promote adhesion of mammalian cells to culture dishes (Table 4 at column 10). Benedict teaches that the amount of FBS (and, therefore, BSA) is optimizable based on the requirements of a given application (column 9, lines 52-54).

A person of ordinary skill in the art would have had a reasonable expectation of success in culturing the 3T3 mouse embryonic lung fibroblasts of Yamamoto to yield a feeder layer by culturing the cells in a medium comprising serum albumin, insulin, and Medium 199 because Goodheart and Hook teach that similar cells (human embryonic lung fibroblasts) can be cultivated in such a medium. Substituting the BSA of Goodheart and Hook for the FBS of Yamamoto would have constituted routine optimization, the skilled artisan recognizing that Benedict teaches that both of these agents promote cell

adhesion. The skilled artisan would have been motivated to include insulin in the medium of Yamamoto because Reich teaches that insulin promotes proliferation.

Determining the amount of BSA and insulin to include in the medium of Yamamoto would have constituted routine optimization, since Benedict teaches that the amount of FBS (and, therefore, BSA) may be modified to suit downstream applications and since Reich teaches that insulin promotes cell proliferation. Because the goal of Yamamoto's method is to produce a confluent feeder layer adhered to a culture dish (paragraph 3, e.g.), determining the amount of BSA to promote adhesion, the amount of insulin to promote proliferation (and, therefore, formation of a continuous sheet), and the number of doublings to permit the cells to undergo would all have constituted routine optimization.

A person of ordinary skill in the art would have had a reasonable expectation of success in culturing the 3T3 lung fibroblasts of Yamamoto in a medium comprising a cell adhesion factor, e.g. collagen, because Hook teaches that similar cells may be cultured with collagen hydrogels. The skilled artisan would have been motivated to include a cell adhesion factor because Hook teaches that similar cells preferentially attach to collagen (Figures 6C and 6D; paragraphs 143-144).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to substitute varying amounts of the BSA of Hook and Benedict for the FBS in the medium of Yamamoto; to include the insulin of Hook, Goodheart, and Reich in the medium of Yamamoto; and to include the collagen of Hook in the culturing method of Yamamoto because Goodheart and Hook suggest including

these components and because Benedict and Reich suggest optimizing the amounts of these components.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 5 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto, Goodheart, Hook, Reich, and Benedict as applied to claims 1-4, 6-9, 11-15, 17, and 18 above, and further in view of Tang et al. (2004, U.S. Patent Application Publication 2004/0059098; reference G).

The teachings of Yamamoto, Goodheart, Hook, Reich, and Benedict are relied upon as above. Yamamoto, Goodheart, Hook, Reich, and Benedict do not suggest including epithelial cell growth factor (EGF) in the media.

Tang teaches that EGF promotes proliferation of human lung fibroblasts (paragraphs 333 and 335).

A person of ordinary skill in the art would have had a reasonable expectation of success in including the EGF of Tang in the medium of Yamamoto in view of Goodheart, Hook, Reich, and Benedict because Tang teaches that mammalian lung fibroblasts may be cultured with EGF. The skilled artisan would have been motivated to include EGF because Tang teaches that this growth factor promotes proliferation of fibroblasts.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto, Goodheart, Hook, Reich, and Benedict as applied to claims 1-4, 6-9, 11-15, 17, and 18 above, and further in view of Wei et al. (2003, U.S. Patent Application Publication 2003/0017485; reference H).

The teachings of Yamamoto, Goodheart, Hook, Reich, and Benedict are relied upon as above. Yamamoto, Goodheart, Hook, Reich, and Benedict do not teach all of the basal media recited in claim 1.

Wei teaches suitable culture media for mammalian cells (paragraph 58).

The selection of the basal mammalian culture media from the list in claim 1 would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Wei teaches that these media are functional equivalents for mammalian cell culture. A holding of obviousness over the cited claims is therefore clearly required.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art

may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims and share an inventor or assignee with the instant application. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651